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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	35

DATE MAILED: 08/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/249011	CO
Examiner	**Art Unit**
GAMBEL	1644

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.

If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.

If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.

Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 2/25/03

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-48, 51-76

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 41-45, 47, 48, 51-63

5)☑ Claim(s) _____ is/are allowed. 1-12, 15, 21, 23, 25, 27, 36, 38, 39, 46, 68-74, 76

6)☑ Claim(s) _____ is/are rejected. 24, 28, 30-35, 40, 64-67, 75

7)☑ Claim(s) 25 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4)☐ Interview Summary (PTO-413) Paper No(s). _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: _____

PAPER NO. 35

DETAILED ACTION

1. Applicant's amendment, filed 2/25/03 (Paper No. 32), has been entered.
Claims 24 and 28 have been amended.

Claims 1-12, 15, 21, 23-25, 27, 28, 30-36, 38-40, 46 and 64-76 are being considered as the elected invention.

Claims 41-45, 47,48, 51-63 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to nonelected invention and/or species

Claims 13-14, 16-20, 22, 26, 29, 37 and 49-50 have been canceled previously

2. Given applicant's amendment and arguments, filed 2/25/03 (Paper No. 32); the claimed "3D1" and "H2F", "III2R" antibodies refer to the antibodies corresponding to the sequences disclosed and cited in the specification. The claimed "3D1", "H2F" and "III2R" antibodies are limited to those sequences disclosed and cited in the specification. Accordingly, the previous rejections under 35 USC 112, first and second paragraphs, with respect to the claimed recitation of "3D1" and "H2F", "III2R" antibodies have been withdrawn.

Applicant's amendment of the specification to recited the nucleic acid and amino acid sequences of the III2R (SEQ ID NOS: 25, 27, 29, 31) and H2F (SEQ ID NOS: 26, 28, 30, 31) variable domains as disclosed in Manheimer-Lory, J. Exp. Med. 174: 1639 (1991).

For the record, applicant is invited to clearly state which SEQ ID NOS. correspond to the 3D1 antibody, set forth in the claims.

3. Given the lack of sufficient motivation in the prior art to employ the framework of the III2R or H2F antibodies in the claimed B7-2-specific antibodies in view of applicant's arguments, filed 2/25/03 (Paper No. 32), the previous rejection under 35 U.S.C. § 103 has been withdrawn.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24, 28 and 64-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated nucleic acids comprising SEQ ID NO: 7, SEQ ID NO: 5 or does not reasonably provide enablement for any "a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 8" (e.g. see claim 24 and dependent claims thereof), "a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 6" (e.g.,see claim 28 and dependent claims thereof), "nucleic acid of a nucleic acid molecule that is substantially identical to claims 24/28 (a)(b)(d) (e.g. see claim 24 and dependent claims thereof), a nucleotide sequence which is the complement of the nucleotide sequences according to claims 24/28 (a)(b) (e.g. see claim 28 and dependent claims thereof).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to use the invention commensurate in scope with these claims.

Given the absence of functional language that the nucleic acids encode an antibody or immunoglobulin that binds B7-2 or contribute to an antibody or immunoglobulin that binds B7-2 in the instant claims, applicant has not provided sufficient direction and guidance as to how the skilled artisan can use the claimed nucleic acids.

In the absence of functional characteristics of nucleic acids encoding B7-2 binding antibodies or immunoglobulins or contributing to an antibody or immunoglobulin that binds B7-2 that are shared by members of the genus of nucleic acids and vectors and host cells that comprise said nucleic acids) encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to enable the genus.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, using the claimed nucleic acids, vectors and host cells encompassed by the claims other than nucleic acids that encode a functional B7-2-specific antibody or immunoglobulin or contribute to a functional B7-2-specific antibody or immunoglobulin would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

6. Claims 30-35, 40 and 75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

The claims recite a "fused gene" (vectors and host cells).

The instant specification discloses that "the gene comprises a nucleotide sequence encoding a CDR derived from a light and/or heavy chain of a nonhuman antibody having binding specificity for B7-2 and a framework derived from a light and/or heavy chain of a human origin" (see page 4, paragraph 2 of the specification).

According to Genes IV (Lewin et al, Oxford University Press, page 810, 1990), a gene is defined as "the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding regions (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons).

Since the claims recite "a fused gene", there is insufficient direction and guidance in the specification on how to make and use all of the elements, including the regulatory elements associated with the claimed "fused gene".

For example, immunoglobulin genes comprise various variable and constant region gene elements. In addition, immunoglobulins can be regulated at levels of mRNA transcription, processing, transport stability and translation.

However, there is insufficient direction and guidance as to the nature and characteristics of the claimed "fused gene", including the lack of guidance and direction on how to make and use various gene elements other than CDR and framework nucleic acids to make an antibody or immunoglobulin that binds B7-2.

Further, there is insufficient direction and guidance on how to make and use those "nucleic acids" that are derived from a "CDR" or "light and/or heavy chain". . Also, the invention could embrace any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides found in the reference sequence, which may or may not contribute to an antibody or immunoglobulin that binds B7-2. The instant disclosure has not enabled a sufficient number of species to support the genus of "derived" sequences.

The specification dos not provide a sufficient enabling description of the claimed invention. A person of skill in the art is not enabled to make and use "a fused gene" as recited in the claims. A person of skill in the art would not know which gene elements or sequences are essential, which gene elements or sequences are non-essential in making and using "a fused gene" that produces an antibody or immunoglobulin that binds B7-2. There is insufficient guidance based on the limited disclosure of "a fused gene" in the specification as filed, including very limited information what constitutes "a fused gene" in the specification as filed, to direct a person of skill in the art to select particular gene elements or sequences as essential for making and using an antibody or immunoglobulin that binds B7-2. In addition, a person of skill in the art could not predict which particular gene elements or sequences would be essential and could be used in making a functional antibody or immunoglobulin that binds B7-2.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, making and using "a fused gene" (and vectors and host cells) that would encode an antibody or immunoglobulin that would bind B7-2 would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

7. The following written description rejection is set forth herein.

Claims 30-35, 40 and 75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims recite a "fused gene" (vector and host cells).

The instant specification discloses that "the gene comprises a nucleotide sequence encoding a CDR derived from a light and/or heavy chain of a nonhuman antibody having binding specificity for B7-2 and a framework derived from a light and/or heavy chain of a human origin" (see page 4, paragraph 2 of the specification).

According to Genes IV (Lewin et al, Oxford University Press, page 810, 1990), a gene is defined as "the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding regions (leader and trailer) as well as intervening sequences (introns) between individual coding segments (exons).

Since the claims recite "a fused gene", there is insufficient written description for all of the elements, including the regulatory elements associated with the claimed "fused gene".

For example, immunoglobulin genes comprise various variable and constant region gene elements. In addition, immunoglobulins can be regulated at levels of mRNA transcription, processing, transport stability and translation.

However, there is insufficient written description as to nature and characteristics of the claimed "fused gene", including the lack of written description of gene elements other than CDR and framework nucleic acids.

There is insufficient written description of the sites or elements at which variability may be tolerated and there is insufficient information regarding the relation of structure to function, particularly as it applies to an antibody or immunoglobulin that binds B7-2.

Further, there is insufficient written description with respect to those "nucleic acids" that are derived from a "CDR" or "light and/or heavy chain". There is insufficient written description of a sufficient number of species to support the genus of "derived" sequences. Also, the invention could embrace any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides found in the reference sequence, which may or may not contribute to an antibody or immunoglobulin that binds B7-2.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genuses of "fused genes" and "derived" sequences , and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient to describe the genuses. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genuses as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides (proteins) and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.
Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Therefore, there is insufficient written description with respect to the "fused genes" (vectors and host cells) encompassed by the claimed invention which meets the written description provision of 35 USC 112, first paragraph.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.

8. Claim 25, line 4 is objected because "muring" should be "murine".

9. Claim 1-12, 15, 21, 23, 25, 27, 36, 38, 39, 46, 68-74 and 76 are considered allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Phillip Gambel, Ph.D.
Primary Examiner
Technology Center 1600
August 18, 2003